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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,943	04/14/2004	Matthew P. Collis	P-5667	9041
26253	7590	10/18/2006	EXAMINER	
DAVID W. HIGHET, VP AND CHIEF IP COUNSEL BECTON, DICKINSON AND COMPANY 1 BECTON DRIVE, MC 110 FRANKLIN LAKES, NJ 07417-1880			POHNERT, STEVEN C	
		ART UNIT	PAPER NUMBER	
			1634	

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/825,943	COLLIS, MATTHEW P.	
	Examiner Steven C. Pohnert	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 07 August 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-18 and 29 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 19-28 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 14 April 2004 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Claims 1-18 and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/7/2006.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is recites, "a 5' terminus", in reference to a first oligonucleotide and "a 3' terminus" of a second oligonucleotide. However, the 5' terminus is relative, in that any nucleotide is 5' as long as it has a nucleotide 3' to it. The recitation of "a terminus" is indefinite because it is unclear if the term requires the 5' terminus of the oligonucleotide, or if it encompasses any 5' region in the oligonucleotide without including the 5' terminal nucleotide.

Claim 21 recites, "Amplifying the second oligonucleotide." However, it unclear where in claim 19, this step occurs

4. Claim 22 recites the limitation "of said second portion" in the third line of the claim. There is insufficient antecedent basis for this limitation in the claim. There is no second portion recited in prior claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 19-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nadeau et al (US Patent 5846726) in view of Heller et al (US Patent 6416953).

With regards to claim 19, Nadeau et al teaches a signal primer is initially single-stranded and remains single-stranded in the absence of target; the restriction endonuclease recognition site is not cleavable by the restriction endonuclease. As a result of target-dependent synthesis of a complementary strand, however, the signal primer and its RERS are rendered double-stranded, making the RERS cleavable or nickable by the restriction endonuclease. Cleavage separates the two dyes and the fluorescence intensity of the first dye increases (i.e., quenching is decreased) as an indication of the presence of the target sequence (see column 3, lines 39-55 and figure 1).

With regards to claim 20, Nadeau teaches in figure 1 a detector oligonucleotide forms a DNA duplex with S2 oligonucleotide.

With regards to claim 21, Nadeau teaches extension of both the amplification primer (second oligonucleotide) and signal primer (see column 6, line 14-16). This would encompass amplifying a second oligonucleotide.

With regards to claim 22, Nadeau teaches the use of a signal primer and amplification primer to amplify a nucleotide, followed by hybridization of a second signal primer (see column 6, line 30).

As a portion is not defined in the specification, the references to a second and third portion of claim 23 will be given the broadest reasonable interpretation as being any part of the whole nucleotide.

With regards to claim 23, Nadeau teaches the amplification primer comprises a recognition site for a restriction endonuclease near its 5' end (see column 4, lines 46-47). The amplification primer of Nadeau is a second oligonucleotide.

With regards to claim 24 and 25 Nadeau teaches strand displacement amplification (see column 4 line 42- column 5, line 6).

With regards to claim 26, Nadeau teaches monitoring changes in fluorescence from donor. Detecting fluorescence from a donor is monitoring its emission.

With regards to claim 27, Nadeau teaches use of fluorescein and DABCYL as a fluorophore/quencher pair (see column 9, lines 30-32).

With regards to claim 28, Nadeau teaches the use of bumper primers (a) (see column 5, line 23) and SDA (a-f) (see column 4 line 42- column 5, line 6). Nadeau further teaches the use of a second signal primer, having a restriction enzyme recognition site, and extending it following hybridization (see column 6, line 30) and detection. Nadeau teachings thus encompass amplification by SDA followed by extension of a signal primer, which is cleaved by a nuclease to detect a target nucleotide.

Nadeau does not teach the use of 2 or more fluorophore/quencher pairs.

The specification teaches a quencher can also be a fluorophore (see page 2, lines 19-20). The broadest reasonable interpretation of the claims would thus encompass a signal oligonucleotide with 4 at least fluorescent moieties.

However, Heller teaches in figure 2A a polynucleotide with at least 4 fluorescent moieties. Heller teaches the use of multiple fluorophores results in enhanced fluorescent emission and thus a better signal (see column 9, line 4-12).

Therefore it would have been *prima facie* obvious to one of skill in the art at the time the invention was filed to improve Nadeau method of detecting a target nucleotide by using at least 4 fluorescent labels as taught by Heller, because Heller teaches it enhances the fluorescent signal. The skilled artisan would be motivated to improve Nadeau's method with Heller's multi-labeled oligonucleotide because Heller teaches it enhances fluorescent intensity.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 19, 24-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 12, 13, 14, 34, of U.S. Patent No. 5846726 in view of Heller et al (US Patent 6416953). Although the claims are not identical they are not patentably distinct, as they are co-extensive in scope.

Claim 19 of instant is drawn to a detection of a target nucleotide by extending a detector nucleotide with at least 2 pairs of donor fluorophore/quencher fluorophore pairs separated by a restriction site, extending the duplex, cleaving, and detecting fluorophore. Claim 1, 13, 34 of '726 teaches extending a detector nucleotide with donor fluorophore/quencher fluorophore pairs separated by a restriction site, extending the duplex, cleaving, and detecting fluorophore.

Claims 24 and 25 of instant application are drawn to strand displacement amplification. Claim 14 of '726 teaches SDA.

Claim 26 of instant application is drawn to measuring fluorescent emission. Claim 4 of '726 teaches detection of fluorescent intensity, which is fluorescent emission.

Claim 27 of instant application is drawn to fluorescein/DABCYL. (Claim 12 of '726).

The claims of instant application do not teach or not teach the use of 2 or more fluorophore/quencher pairs.

The specification teaches a quencher can also be a fluorophore (see page 2, lines 19-20). The broadest reasonable interpretation of the claims would thus encompass a signal oligonucleotide with 4 at least fluorescent moieties.

However, Heller teaches in figure 2A a polynucleotide with at least 4 fluorescent moieties. Heller teaches the use of multiple fluorophores results in enhanced fluorescent emission and thus a better signal (see column 9, line 4-12).

Therefore it would have been *prima facie* obvious to one of skill in the art at the time the invention was filled to improve '726 method of detecting a target nucleotide by using at least 4 fluorescent labels as taught by Heller, because Heller teaches it enhances the fluorescent signal. The skilled artisan would be motivated to improve '726's method with Heller's multi-labeled oligonucleotide because Heller teaches it enhances fluorescent intensity.

9. Claims 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 8, and 21, of U.S. Patent No. 6054279 in view of Heller et al (US Patent 6416953). Although the claims are not identical they are not patentably distinct, as they are co-extensive in scope.

Claim 19 of instant is drawn to a detection of a target nucleotide by extending a detector nucleotide with at least 2 pairs of donor fluorophore/quencher fluorophore pairs separated by a restriction site, extending the duplex, cleaving, and detecting fluorophore. Claims 1, 8, 21 '279 teaches extending a detector nucleotide with fluorescent nucleic acid, extending the duplex, cleaving, and detecting fluorophore. Claim 3 teaches fluorescent label comprises a donor and acceptor dye.

Claim 26 of instant application is drawn to measuring fluorescent emission.

Claim 4 of '279 teaches detection of fluorescent intensity, which is fluorescent emission.

The claims of instant application do not teach not teach the use of 2 or more fluorophore/quencher pairs.

The specification teaches a quencher can also be a fluorophore (see page 2, lines 19-20). The broadest reasonable interpretation of the claims would thus encompass a signal oligonucleotide with 4 at least fluorescent moieties.

However, Heller teaches in figure 2A a polynucleotide with at least 4 fluorescent moieties. Heller teaches the use of multiple fluorophores results in enhanced fluorescent emission and thus a better signal (see column 9, line 4-12).

Therefore it would have been *prima facie* obvious to one of skill in the art at the time the invention was filed to improve '279's method of detecting a target nucleotide by using at least 4 fluorescent labels as taught by Heller, because Heller teaches it enhances the fluorescent signal. The skilled artisan would be motivated to improve '279's method with Heller's multi-labeled oligonucleotide because Heller teaches it enhances fluorescent intensity.

10. Claims 19, 24-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 12, 14, and 15, of U.S. Patent No. 5919630 in view of Heller et al (US Patent 6416953). Although the claims are not identical they are not patentably distinct, as they are co-extensive in scope.

Claim 19 of instant is drawn to a detection of a target nucleotide by extending a detector nucleotide with at least 2 pairs of donor fluorophore/quencher fluorophore pairs

separated by a restriction site, extending the duplex, cleaving, and detecting fluorophore. Claim 1, 14 of '630 teaches extending a detector nucleotide with donor fluorophore/quencher fluorophore pairs separated by a restriction site, extending the duplex, cleaving, and detecting fluorophore.

Claims 24 and 25 of instant application are drawn to strand displacement amplification. Claim 15 of '630 teaches SDA.

Claim 26 of instant application is drawn to measuring fluorescent emission.

Claim 4 of '726 teaches detection of fluorescent intensity, which is fluorescent emission.

Claim 27 of instant application is drawn to fluorescin/Rhodamine X. (Claim 12 of '630).

The claims of instant application do not teach not teach the use of 2 or more fluorophore/quencher pairs.

The specification teaches a quencher can also be a fluorophore (see page 2, lines 19-20). The broadest reasonable interpretation of the claims would thus encompass a signal oligonucleotide with 4 at least fluorescent moieties.

However, Heller teaches in figure 2A a polynucleotide with at least 4 fluorescent moieties. Heller teaches the use of multiple fluorophores results in enhanced fluorescent emission and thus a better signal (see column 9, line 4-12).

Therefore it would have been *prima facie* obvious to one of skill in the art at the time the invention was filed to improve '726 method of detecting a target nucleotide by using at least 4 fluorescent labels as taught by Heller, because Heller teaches it enhances the fluorescent signal. The skilled artisan would be motivated to improve

'726's method with Heller's multi-labeled oligonucleotide because Heller teaches it enhances fluorescent intensity.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Steven Pohnert


Jehanne Sittton
JEHANNE SITTTON
PRIMARY EXAMINER

10/6/06